

Research evaluation

EVALUATION REPORT OF THE UNIT GLY-CRRET - Glycobiologie, croissance cellulaire, réparation et régénération tissulaire

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS: Université Paris-Est Créteil Val de Marne

EVALUATION CAMPAIGN 2024-2025 GROUP E

Rapport publié le 10/02/2025

High Council for evaluation of research and highter education



In the name of the expert committee :

Sylvie Ricard-Blum, chairwoman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the president of Hcéres.



Pour faciliter la lecture du document, les noms employés dans ce rapport pour désigner des fonctions, des métiers ou des responsabilités (expert, chercheur, enseignant-chercheur, professeur, maître de conférences, ingénieur, technicien, directeur, doctorant, etc.) le sont au sens générique et ont une valeur neutre.

Ce rapport est le résultat de l'évaluation du comité d'experts dont la composition est précisée ci-dessous. Les appréciations qu'il contient sont l'expression de la délibération indépendante et collégiale de ce comité. Les données chiffrées de ce rapport sont les données certifiées exactes extraites des fichiers déposés par la tutelle au nom de l'unité.

MEMBRES DU COMITÉ D'EXPERTS

Chairperson:	Mrs. Sylvie Ricard-Blum, Université Claude Bernard Lyon 1 - UCBL		
Experts:	Mrs. Christine Chatellard, Université Grenoble Alpes- UGA (representative of supporting personnel) Mr. Rémy Poupot, Université Toulouse 3 Paul Sabatier (representative of CNU)		

HCERES REPRESENTATIVE

Mrs. Anne Marie Di Guilmi

REPRESENTATIVE OF SUPERVISING INSTITUTIONS AND BODIES

Mrs. Carole Henique, Université Paris-Est Créteil Val de Marne



INFORMATION ON THE UNIT

- Name: Glycobiology, Cell Growth and Tissue Repair and Regeneration
- Acronym: Gly-CRRET
- Label and number: EA Upec 4397

Composition of the executive team: Professor Dulce Papy-Garcia (Director). No deputy director and no executive team are mentioned in the document.

SCIENTIFIC PANELS OF THE UNIT

The research topics of the unit are included in the Life Sciences and environment panel (SVE) with a focus on panel SVE3, namely biomolecules, integrative biology, cell biology and development for animal science.

THEMES OF THE UNIT

The unit possesses an internationally recognised expertise in sulphated glycosaminoglycans (GAGs) and in their biosynthetic enzymes. Its global scientific objective is to understand the roles of heparan sulphate proteoglycans (HSPGs) and their synthesis machinery in health and disease with a focus on Alzheimer's disease (AD) and osteoarthritis (OA). This objective defines the 'Brain' and 'Joint' axes of the unit. These diseases being both age-related, the unit also investigates the role of HS during senescence. In addition to the study of molecular mechanisms, the unit develops therapeutic and diagnostic applications, in close collaboration with academic laboratories, clinicians, private companies.

Furthermore, a start-up, Glycanix, was created in 2017 and got the licenses of two patents of the unit (2013 and 2017) to identify inhibitors of heparan sulphate 3-sulfotransferases (HS3STs) and specific HS mimetics for Alzheimer's disease using artificial intelligence and bioinformatics.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The CRRET laboratory was created in 1991 at the now University Paris Est Créteil (Upec) by Professors Denis Barritault and Jean-Pierre Caruelle. It was affiliated with both the University and the CNRS from 1999 to 2009. It then became an 'Équipe d'Accueil Conventionnée CNRS' (EAC-CNRS) with two different directors, Dr. José Courty (CNRS research director) from 2010 to 2015 and Professor Dulce Papy-Garcia from 2015 to 2020. When the CRRET cancer group headed by Dr. José Courty moved to the Mondor Institute for Biomedical Research (IMRB, U955 Inserm, Upec), CRRET became Gly-CRRET, lost the CNRS affiliation and became a research unit affiliated to Upec only. The unit (900 m²) is located in the P1 building of the Upec Faculty of Sciences and Technology connected to an extension in the P2 building on the Upec campus.

RESEARCH ENVIRONMENT OF THE UNIT

The Gly-CRRET unit belongs to the Faculty of Science and Technology and its research activities are integrated into one of the six major themes of Upec entitled "Health, Society, Environment" (axis 4). Several members of the unit participates in Upec councils such as those of the graduate school LIVE, the Doctoral School UPE (ED 402), the Faculty of Sciences and Technology (Scientific Council and Department of Biology), and in Upec committees (e.g., Scientific Evaluation and Management Councils and F3SCT (Formation Specialisée en Matière de Santé, Securité et Condition de Travail). The members of the unit are thus deeply involved in the functioning of the Faculty of Sciences and Technology, doctoral studies and Upec. In addition, the unit has close links with the Rheumatology Department of Henri Mondor Hospital located in Créteil, where two members of the unit work as clinicians providing patient samples used for the investigations carried out mostly in the 'Joint' axis of the unit.

The assistant and full professors of Gly-CRRET are involved in teaching from the first year of Bachelor to the second year of Master programs on the campus where the unit is located. A member of the unit is co-responsible of the specialty "BIOmics" (Bioinformatique et Ingénierie multiomique en Santé et Environnement) integrated into the Master program 'Sciences et Technologie de l'Agriculture de l'Alimentation et de l'Environnement' (STA²E), and the other members of Gly-CRRET are responsible for a number of teaching units and/or practical courses at Upec. The interplay between teaching and research is reinforced by the fact that Master students have access to Gly-CRRET platforms.

Gly-CRRET has developed and maintains numerous analytical platforms including the Glyco-Mix platform dedicated to GAG analysis, animal, confocal microscopy imaging, cell culture and ImHOTeP histological analysis facilities together with facilities for biochemistry and physiology (i.e., Western blot, molecular biology, radioactivity, and patch clamp). These technical facilities share an open space and open access for the members of the unit.



The equipment of the Gly-CRRET platforms are included in the database where all the equipments of Upec labs are inventoried. Several platforms (Glyco-Mix, Histology ImHOTeP, and microscopy) provide services to Upec or other local Research units (IMRB, LEESU, IEES, LISA, OSU).

Part of the space is dedicated to OTR3, a biotechnology company which has been created by the founders of the laboratory and develops medical devices based on tissue regeneration. Two OTR3 employees work at Gly-CRRET and a third one works part-time in Gly-CRRET laboratory. The head of the unit is a consultant of OTR3.

Gly-CRRET research topics are integrated into one of the six major themes of Upec entitled "Health, Society, Environment" (axis 4). Furthermore, it interacts with other Upec research units via its platforms and collaborative projects, for example, with a unit working on polymers and nanoplastics in the context of the Upec environment axis. Gly-CRRET is thus fully integrated in its research environment at the levels of the Faculty of Sciences and Technology and of the University.

Effectifs Catégories de personnel Professeurs et assimilés 4 5 Maîtres de conférences et assimilés Directeurs de recherche et assimilés 1 Chargés de recherche et assimilés 0 Personnels d'appui à la recherche 6,5 Sous-total personnels permanents en activité 16,5 Enseignants-chercheurs et chercheurs non 2 permanents et assimilés Personnels d'appui non permanents 8 Post-doctorants 1 Doctorants 4 Sous-total personnels non permanents en 15 activité

UNIT WORKFORCE on 31/12/2023

Total personnels

The unit welcomed twelve PhD students during the evaluation period, seven (58%) came from other universities than Upec including one from Argentina. Eight (67%) PhD students were supervised by the director of the unit, and four (33%) by another professor. Nine out of the twelve PhD students (75%) were co-supervised. The clinicians contribute to PhD supervision. The document does not mention the unit policy to help young researchers to prepare their accreditation to supervise research, which would allow them to act as PhD supervisors in the future but this point has been addressed by the head of the unit during her presentation. It is difficult to determine the number of postdoctoral fellows who worked in the unit during the evaluated period because different numbers are mentioned in the document, i.e., seven on page 31 whereas nine are listed on page 36 including four postdoctoral fellows and five PhD students who stayed in the unit as postdoctoral fellows after their PhD defence. A comprehensive list of all the postdoctoral fellows with their funding and the date of the start and end of their contract would have been useful. During the visit, the number of four external postdoctoral fellows recruited by the unit during the evaluated period because fellows recruited by the unit during the evaluated period has been specified.

31,5



DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER on 31/12/2023. Employers others than UPEC are grouped under the heading "others".

Nom de l'employeur	EC	С	PAR
UPEC	9	0	6
AUTRES	0	1	0
Total personnels	9	1	6

GLOBAL ASSESSMENT

The unit is organised as a single team and investigates the roles of sulphated glycosaminoglycans (GAGs), mostly heparan sulphate (HS), and their biosynthetic enzymes in health and diseases, i.e., neurodegenerative and arthritic diseases, which define two axes. Given that these diseases are age-related, the unit also includes ageing in its research projects. Gly-CRRET scientific axes and global strategy are extremely well summarised in Figure 2 of the document. The global assessment of the unit is excellent for the functioning (although the administrative support should be improved with Upec help), for its scientific objectives, scientific production and attractiveness. The integration of the research activities of the unit in society is supported by its focus on two major human diseases with unmet therapeutic needs in collaboration with clinicians from the nearby hospital (Hôpital Henri Mondor, Créteil, and Hôpital La Salpétrière, Paris) and with companies, ranging from start-ups (OTR3 and Glycanix) to big pharmaceutical companies such as Johnson & Johnson/Janssen, IBSA (Institut Biochimique SA) and Regen Lab. Furthermore, the research activities, driven by the development of anti-neurodegenerative and anti-osteoarthritic drugs, has led to one patent and two declarations of invention. The Integration of the unit research in the society is thus outstanding.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendation: The size of the subgroups led by different PIs and the distribution of the planned projects should be considered by the director to ensure an even progressing of all researchers, especially in consideration on the heavy teaching duties for some of the PIs.

The unit has been reorganised as a single team with two major clearly defined axes focused on brain and joint respectively. The size of the staff working in both axes varies depending on the success rate to grant applications. All members of the unit, including early-career researchers, submit grant applications.

Recommendation: The unit may consider reinforcing its strategic research plan by selecting their most innovative topics to bring them to a level of international outstanding.

The unit does no longer work on nuclear HS or on cancer but focused on HS, HSPGs and their biosynthetic enzymes in brain and joint, which defines two major axes. Within these axes 3-sulphated HS, a rare modification of HS, and biosynthetic enzymes are studied in relation to the susceptibility to diseases and the characterisation of HS and HSPG biosynthetic machinery was added to the characterisation of HS extracted from cells and tissues using spatial transcriptomics and single cell and single-nucleus RNAseq analyses.

Recommendation: One of the critical experiments is to examine the molecular structure of HS expressed in pathological tissues, which can be anticipated requiring further methodological developments, e.g., HPLC coupled with mass spectrometry.

The unit has created the Glyco-Mix-Mass spectrometry platform and developed mass spectrometry protocols to analyse HS and CS disaccharides in healthy and diseased tissues. However, the mass spectrometer installed thanks to Upec financial support does not appear in the material listed on the web site of the platform, which should be updated.

Recommendation: Most importantly, the unit needs to recruit highly meriting co-workers, which will greatly fortify the development of the unit, regarding research quality and productivity.

The unit has recruited two assistant professors and another has got a permanent contract to strengthen the research activities of the unit. Two experienced researchers, one from the Brain Institute in Paris (full time), and the other one, an expert in GAG-protein interactions, from the University of Liverpool (UK) (part-time, up to 60%) will join the unit in 2025.



Recommendation: It is recommended that the unit should set up more national and international academic collaborations to ensure the positive development of this unit that has a strong potential to stand out as a world-leading research centre within the area of glycobiology and heparan sulphate biology.

The unit has coordinated an international consortium of eight partners (ArrestAD, Stop Alzheimer's Disease, https://arrestad.wordpress.com/welcome/) created in 2017. In addition, there is the opportunity to extend Gly-CRRET research to the National Autonomous University of Mexico (Unam, the biggest university in Latin America) which is implementing the research strategy developed by Gly-CRRET for other neurodegenerative diseases. An international agreement should be signed between, Gly-CRRET-Upec and UNAM.

The unit has successfully implemented most of the recommendations suggested in the previous evaluation as detailed above, and plans to create a new international collaboration with the National Autonomous University of Mexico. The strategy to increase its national and international collaborative networks is based on writing proposals of collaborative projects, and their submission every year to national or European funding agencies and charities.

B - EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the scientific objectives of the unit

The objectives of the unit aim at deciphering the role of GAGs, mostly HS, and their biosynthetic enzymes in two age-related diseases with unmet therapeutic cure, which affect millions of people worldwide (i.e., Alzheimer's disease and related dementia and osteoarthritis and related musculoskeletal disorders), and in development and senescence. Its ultimate goal is to design glycan-based therapeutic and diagnostic strategies. The scientific objectives of Gly-CRRET, based on its strong, nationally and internationally recognised, expertise in GAGs and their biosynthetic enzymes, are excellent.

Assessment on the unit's resources

The unit has an excellent record of successful funding applications at the national and international levels both from governmental agencies, private companies and charities. There is a very good balance between researchers and personnel (technicians, and engineers) supporting research activities. The unit benefits from a strong Upec support resulting in the recruitment of three permanent personnel (two assistant professors and a technician) during the period.

Assessment on the functioning of the unit

The unit adheres to and implements the Upec policy for sustainable development and social responsibility but also promotes additional actions at its own level. The gender balance is excellent and the unit takes care of the working conditions, health, and safety of its staff. The solidarity within the unit appears to be very strong, and is very important for those facing problems.

1/ The unit has set itself relevant scientific objectives

Strengths and possibilities linked to the context

The unit has four objectives. The first one is the development of glycan biology-based tools to fulfil its research goals, the second one aims at studying the role of GAGs and their biosynthetic enzymes in physiopathology, namely Alzheimer's disease and related dementia, osteoarthritis and related musculoskeletal disorders. The third objective focuses on the role of HS in development and senescence. The fourth one is dedicated to glycan-based therapeutic and diagnostic strategies. The ultimate goal of the research performed by the unit is the translation to the clinics. This is the reason why the unit develops three therapeutic approach targeting HS biosynthetic enzymes. The unit collaborates with biotech and pharmaceutical companies and clinicians, creates start-ups and is funded by charities and foundations focused on joint and brain diseases, including Alzheimer's disease, arthritis and Sanfilippo syndrome, a rare childhood neurodegenerative disease, due to a defect in HS degradation. The unit has created the numerous tools and platforms required to achieve these



objectives, and regularly develops new ones. It has for example setup protocols to analyse the composition of HS and CS disaccharides by mass spectrometry during the evaluated period. The unit is thus able to perform a multiscale analysis at the molecular, cellular and tissue levels in agreement with its objectives.

Weaknesses and risks linked to the context

No major scientific weaknesses and risks have been identified

2/ The unit has resources that are suited to its activity profile and research environment and mobilises them

Strengths and possibilities linked to the context

The unit collected about 4 083 k€ from research grants (~680 k€/year on average). The funding is mostly dedicated to hiring personnel with temporary positions, postdoctoral fellows and PhD students (~ 8 persons/year for a total cost of about 450 k€/year on average). The unit has thus a budget of about 230 k€/year for the other expenses. As about twenty full-time personnel perform research activities in the lab with about 11.5 k€ year/person. Upec contributes to approximately 13% of the budget. The regular submissions of proposals should secure funding of the unit beyond 2026.

Weaknesses and risks linked to the context

No scientific weaknesses and risks have been identified. The contribution of two researchers coming from the Brain Institute (ICM, Paris) and from the University of Liverpool (UK) will be instrumental to achieve part of the objectives of the unit. The convention between Upec and their institutions allowing them to join the unit should be finalised as soon as possible. The limited number of postdoctoral fellows over the period is likely a strategical choice made by the unit to favour PhD student recruitment. However, its close relations with private companies led to only two PhD thesis students funded by a Cifre with ScreenCell and Regenlab companies. The number of PhD students supported by a Cifre could be increased.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

Four types of meetings are regularly organised by the unit. The weekly meetings include all the members to discuss daily laboratory issues, including hygiene and safety, research projects, and to present scientific results providing exchange opportunities between the axes. External speakers are occasionally invited to present their research. Bimonthly meetings called 'Club des docs', organised by a PhD student, allow sharing know-how on projects coordinated by young researchers in a convivial atmosphere. They have been extended to the PhD students from other laboratories of the Faculty of Sciences and Technology. Scientific strategies, ongoing and future projects and proposals are discussed in monthly meetings of the researchers. The council including all the permanent staff and representatives of PhD students and non-permanent staff meets five times per year to discuss research profiles for open positions, promotions, equipment and the daily life in the unit.

Gly-CRRET adheres to the Upec policy for sustainable development and social responsibility by implementing recommendations related to the prevention of environmental risks and the pursuit of the sustainable development goals. The unit does its best to consider sustainable development when designing research activities and experiments, and to follow the 4R rules (Reduce, Reuse, Replace, and Recycle). It contributes to decreasing the impact of its activities on the environment by reducing the use of plastics, for example. They also collaborate with laboratories working on nanoplastics in the Faculty of Sciences and Technology by developing methods on its Histology Platform ImHOTeP, giving access to equipment for histology, cell culture and microscopy, doing experiments and/or training collaborators and their students.

Human resource management of the unit includes gender parity (58.5% of women during the evaluated period), equal access to training, internal mobility and career development. The unit takes care of the working



conditions, health, and safety of its staff, and of the prevention of psychosocial risks. There is a correspondent in the unit of the Upec Prevention Assistant Network.

Weaknesses and risks linked to the context

The administrative support of the unit does not meet the requirements of this position and the expectations of the unit.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is excellent. The unit has established national and international collaborations through grants and services thanks to its state-of-the art facilities, and coordinated an international European network. Three members of the unit were awarded national and international prizes, and several members of the unit have been invited as speakers in international conferences and foreign institutions.

Strengths and possibilities linked to the context

Gly-CRETT has co-organised in 2019 a national scientific event, an Inserm workshop on 'Glycosaminoglycans Science and Technologies' in collaboration with a team of the Institute of Structural Biology (Grenoble), the Symposium 'Neurosciences France-Mexico' - Actions France Latin America in Neurosciences with the French Society of Neuroscience and Upec in Paris (2021), and the 'Neuro-Diseases session' of the seventh Latin American Glycobiology Congress (2023) in Mexico. The unit has participated in Erasmus modules (Erasmus+ 'Drug Discovery and Development') involving the visit of the unit by international partners and student exchanges, and have been leaders of work packages in national ANR consortia. The director of the unit has coordinated a European FET OPEN RIA project (ArrestAD) obtained in 2017, meaning that the consortium including eight partners from five countries (France, UK, Poland, Spain and the Netherlands) has been built before the evaluated period. The project ended in 2022 but the unit still collaborates with several partners of this project, including the Spanish and Polish partners, and the UK partner, who will join the unit for the next period. This is very positive to expand the international network of the unit. The unit applied to another European call, the EU Joint Programof Neurodegenerative Disease Research (JPND). It was not founded but the unit will submit a revised proposal integrating the reviewer comments when the call opens.

The scientific reputation of the unit is also attested by 98 communications of Gly-CRRET members in national (55 including 4 invitations) and international (43 including 9 invitations) meetings and by editorial activities in Glycoconjugate Journal and Frontiers in Neurosciences.

Several members of Gly-CRRET were awarded prizes. The director of the unit was awarded the 'Sénat' medal in 2021 during the 'Semaine de l'Amérique Latine et des Caraïbes' (SALC 2021) for her research on Alzheimer's disease and her efforts to strengthen the links between the research carried out in France and Mexico. Another member of the unit was nominated Chancellor of Pondicherry University in 2023 for his work and his involvement in strengthening new interactions and collaborations between this university and Upec, and a third member was awarded the Tillman prize from the Arthrose Foundation in 2019 and a Dreamer research fellowship from Novartis Pharma (France).

The unit proposes a list of BIATSS for the Career Progression Plan (i.e., "repyramidages"). The promotions of the staff, also strongly supported by the unit, mostly depend on committees of the Faculty of Sciences and Technology, Upec and to the Ministry of Research, which makes the final decisions. Two members of the unit were promoted during the evaluated period from Technician to Assistant Engineer, from technical assistant to superior level.

The unit has been awarded eighteen local (Upec, SATT), national (7 ANR grants, ANRT, FRM), and international (H2020 FET OPEN RIA, Sanfilippo Children's Foundation) grants. The unit applies every year to competitive calls, both as the project coordinator or as a partner. The Gly-CRRET unit is indeed asked for partnerships for its expertise in glycobiology by both academic laboratories and companies. The unit is thus very attractive through its success in competitive calls for projects and has a very active policy involving young scientists in grant applications. The successful grant applications allow hiring non-permanent staff (~8 per year), to buy equipment and, of course, to make experiments.

The unit has created new tools to analyse GAGs and HS biosynthetic enzymes and developed several facilities, especially the Glyco-Mix platform. In addition to these analytical methods, the unit develops new protocols (e.g., algorithms for the angiogenesis plugin of ImageJ) to analyse angiogenesis assays. All these tools are available to the other Upec laboratories, national and international laboratories and companies through collaborative projects, and partnerships. The unique expertise of the unit in GAGs and their biosynthetic enzymes



has led to collaborations with local (OTR3) and international (Johnson & Johnson/Janssen, Regen Lab) companies. This is altogether a major strength for participating in collaborative projects, and for training personnel, PhD students and postdoctoral fellows.

Weaknesses and risks linked to the context for the four references above

None identified

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production comprises 110 published articles including 53 original articles, eight reviews and 49 clinical interviews, some of them in renowned journals. All personnel categories co-authored articles. The unit promotes open science, and is fully compliant with research integrity and ethics applicable in its research field in agreement with Upec policy.

Strengths and possibilities linked to the context

The unit has published 112 articles, 55 original articles (two of them noted as submitted in the document provided by the unit are not found in PubMed), eight reviews and 49 clinical articles which highlights its translational activities. One patent has been accepted and two declarations of invention have been deposited. The number of articles per investigator is the same as for the previous period (6.3/year). 38% of the scientific articles and 44% of clinical articles were signed as a first or corresponding author, which is close to 50% for each category. An article published in 2022 reporting the development and implementation of a new algorithm for the previously developed Angiogenesis Analyser has more than 200 citations, and was the eighth most uploaded article in the 'Cell and Molecular Biology' section of the journal Scientific Reports. Two members of Gly-CRRET published an article in Nature Review Rheumatology as the first and second/last authors. Members of the unit co-authored four articles in Nature Communications but they were not in significant positions.

There was an average of 3.5 scientific articles per year and per permanent staff (63 papers/18 permanent staff) including researchers, engineers, and technicians, and an average of 2.1 articles per year per assistant and full professors as last authors. All categories of Gly-CRRET personnel co-authored articles. Nine publications related to angiogenesis were co-authored by the engineer, who developed the angiogenesis plugin of ImageJ, as the sole author of Gly-CRRET. Seven out of the eight PhD students who defended their thesis over the period co-authored publications, four of them as first authors.

The Gly-CRRET benefits from Upec policy for Open Science. Gly-CRRET members were trained to use HAL by the Upec 'Service d'Appui et de Valorisation de la recherche'. The unit aims at integrating its scientific production in HAL. All the articles of the unit are published in Open access, and the Article Processing Charges are supported by the unit grants. Gly-CRRET has adopted the principles of the French National Code of Ethics for Research Professions, which is consistent with the reference framework of the European research and innovation program that the unit has signed. The unit complies with the principles of ethics and research integrity.

Weaknesses and risks linked to the context for the three references above

The unit members who co-authored articles published in high-ranked journals are in significant positions in only one publication.



Assessment on the inclusion of the unit's research in society

The unit has long-lasting and successful collaborations with companies from start-ups to big pharmas, hosts employees of one of them (OTR3), and has deposited one patent and two invention disclosures over the period. It plans to create a new start-up to benefit from financial support to valorise the products issued from its three therapeutic strategies.

Strengths and possibilities linked to the context

The Gly-CRRET has released in 2023 one patent on inhibitors targeting the interaction of internalised 3S-HS with the Tau protein and reducing the aggregation and deposition of this protein. The patent has been developed and deposited in close collaboration with the University Jules Verne Picardie which provided synthetic oligosaccharides. The patent has been accepted, and two invention disclosures related to new therapeutic strategies for Alzheimer's disease and osteoarthritis are being processed.

The unit has established close collaborations with the non-academic world at the national and international levels with companies such as Regenlab (France) and Johnson & Johnson -Janssen (Belgium) to study neural HS 3-O-sulfotransferases and with charities such as France Alzheimer, the Foundation for Medical Research (France) and the San Filippo Children's Foundation (Australia). The director of the unit works as a consultant for Glycanix and OTR3, which further strengthen the links between Gly-CRRET and the companies it is working with.

The unit is also very active in creating start-ups to translate its findings into potential drug candidates. OTR3 and Glycanix have been created before the evaluated period but another start-up GlycADix should be created soon. In addition, the unit plans to create a unique start-up with a complete pipeline (Start-up-venture) including extracellular matrix engineering, GAG-protein interaction and enzymatic therapeutic approaches in collaboration with its partners as mentioned in the trajectory.

The scientific axes of the Gly-CRRET are designed to implement a research strategy to study diseases having a strong societal impact on one hand and rare diseases such as Sanfillipo syndrome on the other hand. Several projects of the unit are funded by national (Foundation for Medical Research, Arthritis Foundation, France Alzheimer Association) and international (Foundation Sanfilippo, Australia) charities to benefit research outcomes for the patients. The unit is deeply involved in translational activities thanks to the above grants, to its collaboration with national and international companies, and the creation of start-ups.

A Gly-CRRET member belongs to the "Science avec et pour la société" Department from Upec. The unit has created LinkedIn and X accounts to disseminate scientific information in French and English, and a YouTube channel in 2023 to share seminars or scientific content. The unit also participates in public debates when an opportunity arises such as the invitation in 2021 of the director to a France 24 TV program to discuss about Alzheimer's disease. Additional communication is made by the Upec media communication services.

The strong links established by the unit with start-ups and pharmaceutical companies at the national and international levels secured by grants and attested by articles either published or in preparation are outstanding. The unit benefits from, and participates in, the actions for open science and sustainable development organised by Upec but it also takes action at its own level as detailed above by promoting the use of the 4R rules and open science, which should be highlighted.

Weaknesses and risks linked to the context for the three references above

A web site presenting the organisation, research axes, major scientific achievements, publications, funding sources and the facilities of the unit is missing.

ANALYSIS OF THE UNIT'S TRAJECTORY

Gly-CRRET will continue developing glycobiology-based research on diseases without efficient cure, namely Alzheimer's disease and related rare tauopathies, osteoarthritis and related pathologies such as rheumatoid arthritis and Sanfilippo syndrome (mucopolysaccharidosis IIIA). The unit plans to develop cross-axes projects to study common disease drivers in different tissues, different HS biosynthetic enzymes, different periods of vulnerability, and different timings of disease development. All these activities are in line with Upec axes of



research (Upec Axe 4. EUR LIVE). The unit will further explore GAG-protein interactions by studying HS interactomes using clustering analysis of genetic data across the genome and exploring the effects of genetic risk factors on neurodegenerative, developmental, and joint diseases. This approach will also integrate epigenomic data, as potential mediator of gene-HS interactome interactions, and metabolomic data, allowing for the development of innovative approaches and identification/confirmation of the interest of glycanic biomarkers and drug targets. The contribution of two researchers coming from the Brain Institute (ICM, Paris) and from the University of Liverpool (UK) will be instrumental to ensure the success of the unit trajectory.

The unit will continue collaborating with clinicians and industrial partners to develop its translational activities by exploring the extracellular matrix, GAG-protein interaction and enzymatic therapeutic approaches, and by creating a unique Start-up with a complete pipeline (Start-up-venture) for the diagnostic and therapeutic strategies approaches having demonstrated efficacy in vivo. Gly-CRRET staff will be part of the scientific board of this structure and the CEO will have a business experience.

There has been very preliminary discussion with the Institut Mondor de Recherche Biomédicale (IRMB, U955 Inserm – Upec) for a possible affiliation of Gly-CRRET in the future. This would require further discussions with Upec and Inserm but no affiliation is planned in the next four or five years.

RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

To quickly improve the administration of the unit in close collaboration with the Department of Human Resources of Upec, which is aware of the problem.

Recommendations regarding the Evaluation Area 2: Attractiveness

None

Recommendations regarding Evaluation Area 3: Scientific Production

To improve the leadership of the unit in articles published in high-ranked journal.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

To create a web site to increase the visibility and attractiveness of the research activities of the unit and its platforms.



CONDUCT OF THE INTERVIEWS

Date

Start: 12 December 2024 at 08:00

End: 12 December 2024 at 18:00

Interview conducted: online

INTERVIEW SCHEDULE

Session publique (comité + membres de l'unité + direction + tutelle)

08:15 Accueil et test de connexion

08:30 Présentation des membres du comité et du déroulé de la visite. Pr. Sylvie Ricard-Blum

Présentation du bilan de l'unité

08 40 Présentation globale de l'unité : Ressources humaines, infrastructure, objectifs et axes scientifiques et bilan quantitatif de la période. Pr. Dulce Papy-Garcia (15 min + 15 min questions)

Présentation du bilan par axes scientifiques

09:15 Axe 'Articulation' : présentation des défis, approches scientifiques et résultats majeurs. Pr. Patricia Albanese (20 min + 15 min questions)

09:55 Axe 'Cerveau' : présentation des défis, approches scientifiques et résultats majeurs. Pr. Dulce Papy-Garcia (25 min + 15 min questions)

10:45 Pause

Présentation de la trajectoire

11:15 Introduction à la trajectoire. Pr. Dulce Papy-Garcia

Présentation de la trajectoire par axes et objectifs 11:25 Axe 'Articulation' Pr. Patricia Albanese suivie par l'intervention de Benjamin Even, Florent Eymard (20 min + 15 min questions)

- 12:00 Axe 'Cerveau' Pr. Dulce Papy-Garcia suivie par l'intervention de Alwyn Dady (20 min + 15 min questions)
- 12:35 Déjeuner et discussion interne du comité
- 13:30 Echange avec les chercheurs et enseignants-chercheurs Pr. Sylvie Ricard-Blum
- 14:00 Echange avec les ITA-BIASS Dr. Christine Chatellard
- 14:30 Echange avec les étudiants et les post-docs Pr. Rémy Poupot)
- 15:00 Discussion interne comité
- 15:30 Réunion avec les représentants des tutelles Carole Hénique (Vice-Présidente Recherche UPEC)
- 16:00 Réunion avec la direction de l'unité actuelle et future
- 16:30 Finalisation du rapport (membres du comité)
- 18:00 Fin de la visite

PARTICULAR POINT TO BE MENTIONED

None.



GENERAL OBSERVATIONS OF THE SUPERVISORS



Vice-Présidence de la recherche et de la commission de la recherche : Mme Carole Hénique - VPCR Université Paris-Est Créteil (UPEC) 61, avenue du Général de Gaulle 94010 Créteil France

Affaire suivie par : M. Lionel Casterman Responsable du pôle structuration et stratégie scientifique Tél. +33 (0)1 45 17 71 08 lionel.casterman@u-pec.fr

Créteil, le 3 février 2025

Objet : Observations de portée générale sur le rapport d'évaluation Hcéres - E2026-EV-0941111X-DER-ER-DER-PUR260025173-SVE3-GLY-CRRET (Glycobiologie, croissance cellulaire, réparation et régénération tissulaire)

Nous tenons tout d'abord à remercier la conseillère scientifique qui a accompagné le processus d'auto-évaluation et l'évaluation elle-même pour son écoute et la bienveillance dont elle a fait preuve durant l'ensemble du processus. Nous adressons également nos remerciements les plus sincères aux membres du comité d'experts et à sa présidente pour le rapport d'évaluation du Gly-CRRET dont nous partageons le diagnostic et, pour l'essentiel, les recommandations.

Nous remercions les membres du comité d'avoir souligné les éléments distinctifs du positionnement et des orientations stratégiques du Gly-CRRET avec son identité forte sur les glycosaminoglycanes (GAGs) et leurs enzymes de biosynthèse dans des contextes physiopathologiques comme la maladie d'Alzheimer ou l'ostéoarthrite. Le rapport manifeste l'intérêt des thématiques scientifiques de l'unité de recherche, la qualité de ses objectifs et approches scientifiques, l'augmentation de la qualité de sa production scientifique, le savoirfaire en termes de valorisation de la recherche, le rayonnement international du Gly-CRRET et l'implication du personnel en enseignement.

La direction de l'unité de recherche manifeste sa motivation pour continuer à faire évoluer les marqueurs de qualité au cours de la prochaine période, ce qui est possible grâce à la motivation des chercheurs, à l'implantation des plateformes technologiques portées par le personnel BIATTS, ainsi que par le fort soutien de l'UPEC, notamment sur les problématiques concernant les aspects administratifs.

Nous ne formulons pas d'observations de portée générale sur le rapport d'évaluation de cette unité de recherche.

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Nous prendrons note des recommandations et en tant que tutelle, nous nous efforcerons à soutenir le Gly-CRRET pour lui permettre de répondre aux axes d'amélioration tout en restant attentifs aux enjeux posés par les changements des contextes de la recherche.

Je vous prie d'agréer, Mesdames, Messieurs, mes salutations distinguées.

Carole Hénique

C. CT

Vice-présidente de la recherche et de la commission de la recherche



The Hcéres' evaluation reports are available online: www.hceres.fr

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